



Figure 1: A Primer on Ubiquitination

During the first step of Ub conjugation, ATP is expended as the catalytic cysteine of E1 (Ub activating enzyme) forms a thiol-ester intermediate with the terminal glycine of Ub. Next, Ub is transferred as a thiol-ester bond to the catalytic cysteine of an E2 (Ub conjugating enzyme). Finally, in the presence of an E3 (Ub ligase) Ub is typically transferred to the lysine residue of a target protein via an isopeptide bond.

Proteins can be mono-ubiquitinated or poly-ubiquitinated. The fate of a ubiquitinated protein depends on the type of ubiquitination: mono-ubiquitination of a membrane protein can lead to its internalization. K48-linked poly-Ub tends to target proteins for proteasomal degradation.

